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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,793	11/02/2001	Jacobus Christianus Johannes Stiekema	O/97277 US/D1	3402

31846 7590 07/08/2004

AKZO NOBEL PHARMA PATENT DEPARTMENT
29160 INTERVET LANE
MILLSBORO, DE 19966

EXAMINER	
PAGE, THURMAN K	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 07/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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7590 07/03/2003

WILLIAM M. BLACKSTON
AKZO NOBEL PATENT DEPARTMENT
SUITE 206
1300 PICCARD DRIVE
ROCKVILLE, MD 20850

EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	13

DATE MAILED: ~~07/03/2003~~
Restart 7-8-04

Please find below and/or attached an Office communication concerning this application or proceeding.

Withdrew abandonment & restart action due to change of address filed 6/3/03 wasn't processed in file until 6/4/04.

B. Gray
7/8/04

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 10/005,793	Applicant(s) JOHANNES STIEKEMA ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Applicant's request for continued examination and preliminary amendment, filed on May 28, 2003, is acknowledged.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Regarding claims 11-18, the phrase "administering for each treatment" renders the claims indefinite, because it is not clear whom or what are the compositions administered to.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudo et al. (U.S. Patent 4,331,697) in view of Ahmad et al. (U.S. Patent 5,252,213) and further in view of Petitou et al.(U.S. Patent 5,378,829).

Kudo et al. teaches that biomedical materials, such as vascular catheters, artificial kidneys and extracorporeal circuits for auxiliary circulating devices, which make direct contact with the blood, are used to temporarily conduct the blood out of the body or for substituting body organs with artificial organs (See col. 1, lines 19-30). Kudo et al. teaches that said biomedical materials are made of glass, metal, plastics and rubbers, and it is known that upon contact with these biomedical material the blood coagulates and forms a thrombus on their surfaces, which can stop the blood current or moves with the blood current to cause complications, such as thrombosis or myocardial infraction (See col. 1, lines 31-41). Kudo et al. further teaches that in using these biomedical materials, it is conventional practice to prevent thrombus formation by administering an antithrombotic agent, such as heparin, coumarine or sodium citrate, to render the blood non-clotting, but advices against systemic administration of heparin because of danger of bleeding and provides heparin derivatives as the antithrombotic agents used in the invention (See col. 1, line 41 to col. 2, line 51).

Thus, Kudo et al. provides the general teachings that extracorporeal circuits cause blood clotting upon contact with the blood of a patient and the blood clotting is prevented by the administration of an anticoagulant agent. Kudo et al. is deficient in the sense, that it does not specify whether the extracorporeal blood treatment is chronic and intermittent, and does not include the compounds claimed in the instant application among the antithrombotic agents used in the invention.

Ahmad et al. teaches that hemodialysis treatment is used as a therapeutic measure when a patient's kidneys no longer perform their blood purifying function because of disease or traumatic removal and most kidney failure patients require dialysis treatment three times weekly (See col. 1, lines 44-60). Ahmad et al. teaches that the contemporary dialysis machine has a blood circuit comprising a blood pump, and during treatment, blood is drawn from the patient, pumped into the hemodialyzer and returned to the patient (See col. 3, lines 20-26). Additionally, Ahmad et al. teaches that the dialysis machine comprises a means for adding an anticoagulant to the blood circuit to minimize fibrin ring deposits, and includes heparin fragments among the anticoagulants used in the invention (See col. 5, line59 to col. 6, line 10).

Thus, Ahmad et al. teaches that patients suffering from renal failure, undergo chronic, intermittent extracorporeal blood circuit treatment, and thrombus formation in dialysis machines is prevented by the addition of anticoagulant agents, such as heparin derivatives.

Petitou et al. discloses sulfated glycosaminoglycanoid derivatives of heparin, and the pentasaccharides claimed in claims 11-18 of the instant application among them, and teaches that the compounds have antithrombin and antithrombotic activity and can be administered enterally or parenterally, including by injection, in a daily dosage of 0.001-10 mg. per kg. body weight (See col. 1, line 1 to col. 5, line 5 and examples). The daily dosage disclosed by the prior art is identical to the dosage per treatment claimed by Applicant in claims 11 and 15 of the instant application, and it is in the dosage range claimed by Applicant in claims 12 and 16 of the application.

Therefore, in the absence of unexpected results, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Kudo et al. and Ahmad et al. to device a method for preventing clotting induced by contact of extracorporeal circuit surfaces with the blood of a patient comprising administering to the patient undergoing extracorporeal blood treatment or to the circuit anticoagulant agents, and include the sulfated glycosaminoglycanoid derivatives of heparin disclosed by Petitou et al. as anticoagulant agents. The expected result would have been a successful method for preventing blood clotting in extracorporeal circuits, which would otherwise lead to complications in the patient undergoing extracorporeal blood circuit treatment. Because of the teachings of Kudo et al., that extracorporeal circuits cause blood clotting upon contact with the blood of a patient and the blood clotting is prevented by the administration of an anticoagulant agent., the teachings of Ahmad et al., that patients suffering from renal failure, undergo chronic, intermittent extracorporeal blood circuit treatment, and thrombus formation in dialysis machines is prevented by the addition of anticoagulant agents, and the teachings of Petitou et al., that sulfated glycosaminoglycanoid derivatives have antitrombin and antithrombotic activity and can be administered by injection, one of ordinary skill in the art would have a reasonable expectation that the methods claimed in the instant application would be successful at preventing blood clotting upon contact of blood with extracorporeal circuit surfaces. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

6. Applicant's arguments with respect to claims 11-18 have been fully considered in view of Applicant's amendment, which has limited the claimed method of the invention to blood clotting induced by contact with surfaces in patients undergoing chronic, intermittent extracorporeal blood treatment.

7. Applicant argues that the teaching of Petitou et al. is related to the treatment of venous thrombosis and the inhibition of smooth muscle cell proliferation, and the reference does not suggest coagulation induced by contact with synthetic surfaces. While this argument has been found persuasive in view of Applicant's amendment, it is moot in view of the new grounds of rejection. Specifically (See rejection above), Kudo et al. provides the teachings that extracorporeal circuits cause blood clotting upon contact with the blood of a patient and the blood clotting is prevented by the administration of an anticoagulant agent., and Ahmad et al. provides the teachings that patients suffering from renal failure undergo chronic, intermittent extracorporeal blood circuit treatment, and thrombus formation in dialysis machines is prevented by the addition of anticoagulant agents. The teachings of Petitou et al., that sulfated glycosaminoglycanoid derivatives have antitrombin and antithrombotic activity and can be administered by injection, are considered relevant in view of the teachings of the prior art, that blood clotting is prevented in patients undergoing chronic, intermittent extracorporeal blood circuit treatment by the administration of anticoagulant agents. In fact, because of the antithrombin activity of the sulfated glycosaminoglycanoid derivatives, it would have been obvious to one of ordinary skill in the art to device a method for preventing clotting in an

extracorporeal blood circuit comprising administering the anticoagulant agents disclosed by Petitou et al.

Conclusion

8. Claims 11-18 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

Liliana Di Nola Baron

June 27, 2003

Liliana Di Nola-Baron

Patent Examiner

Art Unit 1615